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## **REMARKS**

### **Status of the Claims**

Claims 34-44 are pending herein, claims 1-33 and 45-57 having been previously canceled without prejudice or disclaimer.

"Cationic" is removed from claim 35 as there is no antecedent basis for this term.

Claims 37 and 39 have been amended to incorporate the limitations of the base claim.

Claim 43 has been amended to make explicit what was previously implicit in the claim—that the microparticle composition provided by the method of claim 34 is an unwashed microparticle composition.

### **Information Disclosure Statement**

An Information Disclosure Statement was filed in the present application on February 10, 2004. The Examiner has considered the US patent references, but not the foreign patent and literature references from the prior case, because they are not in the electronic file. Applicant notes that these references were submitted in the parent application and that they should be available from that application for purposes of electronic scanning. Applicant is making this request due to the number of references that have been submitted and the burden that recopying and resubmitting these references would bring to bear.

### **Rejection of claims under 35 U.S.C. 102 and 103**

Claims 34, 35 and 42-44 are rejected under 35 U.S.C. 102(e) as anticipated by Levy (US 6,395,253). Moreover, claims 36 and 41 are rejected under 35 U.S.C. 103(a) as being anticipated by Levy. The Applicants respectfully traverse these rejections and their supporting remarks.

For example, independent claim 34 is directed to a method of producing a microparticle composition, which method comprises: (a) forming an emulsion comprising (i) a polymer selected from the group consisting of a poly( $\alpha$ -hydroxy acid), a polyhydroxy butyric acid, a polycaprolactone, a polyorthoester, a polyanhydride, and a

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polycyanoacrylate, (ii) an organic solvent, (iii) a detergent and (iv) water; and (b) removing the organic solvent from the emulsion to form microparticles. The microparticles are not subjected to a washing step. Moreover, about 10-90% of the total detergent in the microparticle composition is bound to the microparticles and the remainder is unbound.

As indicated in paragraph 0011 of the present specification, The present inventors have found that adsorption of macromolecules to microparticles can be improved by ensuring that detergent is made available for forming a complex with the macromolecules at the time of adsorption. This availability can be accomplished, for example, by ensuring that the process for producing the microparticles results in a product containing a substantial amount of unbound detergent. This is in contrast with prior art techniques, where microparticles are thoroughly washed to remove residual detergent prior to macromolecule adsorption. For instance, in the Examples found in PCT/US99/17308, the microparticles are washed multiple times with water (i.e., they are washed with water four times by centrifugation) prior to exposure to the macromolecule of interest. Such washing steps remove essentially all unbound detergent, resulting in a final product in which greater than 99% of the remaining detergent is bound to the particles.

In this regard, Levy is somewhat analogous to PCT/US99/17308, because the Example set forth in Levy teaches the following: "The W/O/W emulsion was stirred with a magnetic stirring bar at 4° C. overnight to evaporate the organic solvent. The spheres were recovered by ultracentrifugation (25,000 rpm, 4° C. for 20 min), *washed three times* with 25 ml TE, resuspended in 2 ml ddH<sub>2</sub>O, and the resulting suspension frozen (on dry ice for 30 min) then lyophilized...."

In view of the above teachings, it is respectfully submitted that, one of ordinary skill in the art upon reviewing Levy would have followed Levy's procedures and would have washed the microspheres, thereby producing a product in which more than 90% of the total detergent in the microparticle composition is bound to the microparticles. This is in contrast to claim 34 in which the microparticles are *not* subjected to a washing step,

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and in which about 10-90% of the total detergent in the microparticle composition is bound to the microparticles, and the remainder is unbound.<sup>1</sup>

For at least this reason, it is respectfully submitted that independent claim 34, as well as claims 35, 36 and 41-44 dependent thereon, are neither anticipated by nor obvious in view of Levy.

Accordingly, reconsideration and withdrawal of the rejection of claims 34-36 and 41-44 under 35 U.S.C. 102(e) or 103(a) over Levy are respectfully requested.

#### **Objection to Claims 37-40**

Claims 37-40 are objected to as being dependent upon a rejected base claim, but have been indicated to be allowable if rewritten in independent form, including all of the limitations of the based claim and any intervening claims. By the foregoing amendment, this action has been taken.

Accordingly, it is believed that these claims are now in condition for allowance.

#### **CONCLUSION**

Applicants submit that the claims of the present invention are in condition for allowance, early notification of which is earnestly solicited. Should the Examiner be of the view that an interview would expedite consideration of this Amendment or of the application at large, request is made that the Examiner telephone the Applicant's attorney at (703) 433-0510 to resolve any outstanding issues.

#### **FEES**

The Office is authorized to charge any additional fees required to deposit account number 50-1047.

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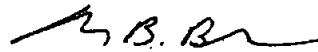
<sup>1</sup> Note also that Levy's technology and motivations are quite different from those of the present inventors in that the biologically active macromolecules of Levy are encapsulated during Levy's microsphere formation process, rather than incubated with the microspheres subsequent to their formation. (See, e.g., claims 43-44.)

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**CORRESPONDENCE**

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Respectfully submitted,



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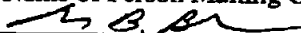
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